AWARD NUMBER: W81XWH-14-1-0043

TITLE: Validating Biomarkers for PTSD

PRINCIPAL INVESTIGATOR: Charles R. Marmar, MD

RECIPIENT: New York University, New York, NY 10016-6402

REPORT DATE: April 2015

TYPE OF REPORT: Annual

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                           Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

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14. ABSTRACT

Validating markers is particularly important, as few biomarkers for PTSD studies have replicated findings following the test results and even fewer have examined the stability of biological markers longitudinally. Those longitudinal studies which have been conducted in PTSD suggest that neural activity may change with symptom trajectories. Longitudinal stress research suggests that other biomarkers may change over time, including gene expression and neuroendocrine functioning. One of the aims of the proposed study is to fill this gap in knowledge, by re-evaluating 70 participants from our original sample (35 PTSD+ and 35 PTSD-) to confirm the stability of biomarkers.

15. SUBJECT TERMS

Veterans, soldiers, Posttraumatic Stress Disorder, PTSD, OIF, OEF, mental health, mental illness, biomarkers, biological markers, trauma, DoD, Department of Defense

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U	UU	22	19b. TELEPHONE NUMBER *(include area code)*

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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

It is imperative to move this research forward towards clinical utility through validation studies including replication of promising markers in newly acquired cases and controls and determination of the stability of the markers in longitudinal studies of participants already enrolled. Validating markers is particularly important, as few biomarkers for PTSD studies have replicated findings following the test results and even fewer have examined the stability of biological markers longitudinally. Those longitudinal studies which have been conducted in PTSD suggest that neural activity may change with symptom trajectories. Longitudinal stress research suggests that other biomarkers may change over time, including gene expression and neuroendocrine functioning. One of the aims of the proposed study is to fill this gap in knowledge, by re-evaluating 70 participants from our original sample (35 PTSD+ and 35 PTSD-) to confirm the stability of biomarkers and their clinical and cognitive correlates in the same sample over time. We predict that our markers will correctly classify those whose diagnostic status is stable over time, those cases who remit, and those controls who develop PTSD at follow-up. In addition to validating diagnostic markers the proposed longitudinal study will accelerate the identification of biological correlates of the various trajectories of PTSD, as well as recovery process. This knowledge may then be translated to not only better identify various stages of the disorder, but also to the development of novel behavioral and pharmacological interventions targeting specific biomarkers at specific time points.

Specific Aims:
1. To validate candidate diagnostic biomarkers for PTSD in Iraq and Afghanistan Veterans from our recently completed discovery phase study. We will accomplish this aim by enrolling 35 new PTSD cases and 50 new controls.
2. To determine the relationship of longitudinal changes of biomarkers with longitudinal changes in diagnosis by reassessing 35 PTSD cases and 35 controls from our recently completed biomarker discovery phase (Time 1). The 35 cases and 35 controls will be reassessed 12 to 24 months after their initial assessment (Time 2).
3. To ascertain biomarkers for PTSD from DoD maintained Archive Sera samples drawn before and after deployment for participants enrolled in the discovery and validation phases of our study.
4. To compare biomarkers for warzone related PTSD in male and female OEF and OIF veterans to determine common vs. gender specific markers and to contribute to the understanding of gender specific pathways for developing PTSD.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Veterans, soldiers, Posttraumatic Stress Disorder, PTSD, OIF, OEF, mental health, mental illness, biomarkers, biological markers, trauma, DoD, Department of Defense

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

OBJECTIVE 1: Planning Phase: Obtain IRB Approval(s) and regulatory requirements to recruit new participants and to receive participants' consent to access to DoD Serum repository.
Timeframe: Months 1-3,
Tasks:
1. Secure IRB approvals and all regulatory requirements from NYU, MSSM, JJPVAMC and HRPO to receive clearance to access data from the DoD Serum repository.
2. Obtain IRB approval to include increase the sample size for validation studies and to re-invite current participants for the stability studies.

Percentage of completion: 100%

OBJECTIVE 2: Recruit eligible participants for validation, collect data.
Timeframe: Months 3-21,
Tasks:
1. Outreach and recruitment via flyers, presentations, website newspaper and television advertisements, informal letters, internet postings, referral
2. To test stability of the markers, recall 35 cases and 35 controls from the Biomarkers discovery phase. Enroll 35 new cases and 50 new controls for the validation study.
3. Data collection on participants at NYUMC - diagnostic evaluation, self-report questionnaires, Neurocognitive testing and post dex blood draw
4. Data collection at MSSM/JJPVAMC on all participants – Blood Draw: genetic, endocrine, metabolic and multi-omics samples
5. Neuroimaging MRI acquisition at NYUMC for all participants, processing at UCSF
6. Entry, filtration, and quality control of collected data – all sites

Percentage of completion: 41% of the overall objective.

OBJECTIVE 3: Obtain Archived Sera from DoD repository and conduct data analysis
Timeframe: Months 7-22,
1. Obtain Archived Sera data, remove PII, and distribute information to appropriate team members for omic studies
2. Pool DoD Sera data with information collected during discovery phase
3. Prepare for data analysis

Percentage of completion: 60%

OBJECTIVE 4: Data Analysis Phase
Timeframe: **Months 8-11**, **Tasks**:
1. Conduct univariate and multivariate analyses to validate biomarkers for PTSD identified in our recently completed discovery phase by ascertaining these biomarkers in a newly recruited sample of 35 cases and 50 controls.
2. Conduct univariate and multivariate analyses to determine the stability of biomarkers for PTSD over one to two years in 35 cases and 35 controls.
3. Conduct univariate and multivariate analyses of biomarkers ascertained in Archived Sera before and after warzone deployment to determine if candidate PTSD diagnostic biomarkers emerge following warzone exposure or are pre-existing vulnerability factors.

Percentage of completion: 0%

OBJECTIVE 5: Disseminate and Report Findings
Timeframe: **Months 11-12**, **Tasks**:
1. Prepare final report of findings to DoD
2. Prepare manuscripts for scientific journals

Percentage of completion: 0%

What was accomplished under these goals?
For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the

project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

During this period of the project the following activities occurred:

1. Communication
The team engaged in bi-weekly communication meetings via teleconference to ensure the successful and timely execution of the planning and Implementation Phase.

Calls took place between the PIs and investigators at each site (SF VAMC, UCSF, Mt Sinai, Bronx VA, Emory University and NYU). Meetings addressed safety issues, clinical questions, strategies for improving subject recruitment and enrollment, strategies for maximizing number of matching participants in gender, ethnicity and age for the participation in study visits, and ensuring that participants moved through all stages of the study quickly and efficiently (in order to avoid attrition). A detailed recruitment plan with quarterly goals for each site was developed and discussed in these meetings. The PIs and investigators also discussed refining the clinical data collected, the imaging and the blood protocols to meet the goals of this research project.

The quarterly meeting took place in Santa Barbara, California in January, 2015. The meeting was organized by the UCSB team, and led by Drs. Charles Marmar and Frank Doyle. Attendees included the MSSM/JJPVAMC team lead by Dr. Rachel Yehuda, UCSF team lead by Dr. Owen Wolkowitz, UCSF/San Francisco VA team member Susanne Mueller, Emory team lead by Dr. Kerry Ressler, ISB team lead by Dr. Lee Hood and the Fort Detrick team led by Dr. Marti Jett and Ron Hoover. During the meeting, the team discussed study progress, challenges and successes of the third quarter, and reviewed recruitment /enrollment efforts, sample management, forming a study advisory board, quality control of study data and sample transfer procedures.

Preparations for the upcoming quarterly meeting that will be held at NYU are currently underway. This meeting will be led by the NYU team and will include all the study cores, as well as legal representatives. The focus of this meeting will be developing a consortium agreement, including patent applications in addition to analysis and manuscript progress, quality control, and recruitment/enrollment.

2. IRB
IRB protocols for the following sites- NYUMC, MSSM, and JJPVAMC- are approved for this study period. These are the recruiting sites for this study and are the only sites with access to PHI information. All other sites receive only de-identified data and therefore are exempt from this process. Due to the overlap between this research project and the Biomarkers for PTSD research project (overlap in study procedures and study participants included in both research project), the IRB application for this project was submitted as an amendment to the Biomarkers for PTSD study. We received IRB approval from all 3 institutions to conduct this study. In February, 2015 an IRB modification was submitted and approved to use an updated MRI brain scanner at NYU's Center for Brain Imagining (CBI). No additional risks/benefits are anticipated from this change, and the scanner is currently being pilot tested for consistency.

3. Databases: Tracking and Management
A secure tracking database was developed for this project to track participants at both recruitment sites. Clinical data from the interview, neurocognitive measures and self-report measures were digitized so that they could be completed digitally and the dataset saved directly onto the study secure SQL database server. All data transfer protocols to the cores (i.e. MRI scans, blood, and urine) were finalized. Remote access/VPN connection was provided to the Bronx site to access the tracking database and SQL server. All imaging data acquired at NYUMC and transferred to USCF is now saved in the study secure database server and is being analyzed using the FSL neuroimaging software.

4. Outreach and Recruitment:

Recruitment strategies and procedures have been established and coordinated between the two recruitment sites. Outreach efforts continue in terms of contacting veteran's organizations and establishing relationships in order to recruit new participants in addition to the participants from the discovery stage. Letters were mailed to participants in the discovery phase to inform them about the validating study. Staff at both sites followed up with phone calls to those participants. A new Director of Veterans Outreach, Craig Vandergoot, was hired in February to lead recruitment efforts

The team worked to continue to work on recruitment ads to specifically target veterans in the area with PTSD. Jared Sterk and Craig Vandergoot from the outreach team are focusing recruitment efforts on establishing relationships with veterans' organizations. The study team continued to respond to calls and electronic inquiries promptly. Enrollment goals and achievements and procedures completed for all four quarters and Year 1 totals across both sites are indicated in the attachment titled, *Biomarkers Recruitment Report Quarterly Tables_Annual Report*. Adjustments have been made to previously reported enrollment numbers to reflect updates from subjects with pending subgroup designations.

5. Obtaining Archived Sera Samples

One of the aims of this study is to ascertain biomarkers in archived sera from 270 participants enrolled in the discovery and validation phases of our study. We forwarded a request to the Armed Forces Health Surveillance Center for 158 participants who enrolled in the discovery phase and consented in this study to access their archived Sera. For each participant we requested multiple samples (~3-4) to include samples from prior to deployment and post deployment. This will enable us to conduct longitudinal assessment of the relationships among biomarkers and PTSD. After obtaining the archived sera, we removed PII, and provided the samples and information to Dr. Marti Jett at Fort Detrick, MD who will carry out omics studies including miRNA markers. After conducting preliminary analysis on these samples we will request the second batch of archived sera samples until we reach the aim of this study (N=250).

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

- The research team, led by Dr. Charles Marmar, participated in biweekly Webinars to discuss presentations related to biomarkers, review scientific progress and guide research objectives. The Webinars included the following topics:

  - Transcriptomics & Epigenetics
  - Proteomics and regulatory miRNAs
  - Metabolism and Cell Aging
  - Neuroendocrine
  - Bioinformatics
  - Neurogenetic
  - Neuroimaging

- Dr. Charles Marmar and NYU study team member, Roland Hart attended the annual meeting for the International Society for Traumatic Stress Conference (ISTSS)

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to Report

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

In the next reporting period:
1) Continue to consent and enroll participants
2) Continue to re-invite participants from the discovery phase into this validating phase to test the stability of the biomarkers
3) Refine implement the refined protocols of blood collection and imaging acquisition and analysis.
4) Continue to administer assessment measures
5) Continue recruiting new participants to test the validity of biomarkers.
6) Continue data collection, entry and data management
Continue biomarkers data collection including blood specimens, imaging, self-report measures, and neurocognitive assessments.

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to Report

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report

commercial technology or public use, including:
- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

> Nothing to Report

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:
- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

> Nothing to Report

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

> This is the fourth quarter of the project and we are continuing the implementation phase. We accomplished our goals during this period. Implementation and recruitment activity is working well and we didn't encounter any issues. We plan to intensify our outreach effort next period to reach our recruitment goals.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

The MRI procedure has been halted temporarily due to the transition from the old magnet to a new magnet at the Center for Brain Imaging. The new magnet is currently being tested for consistency by piloting healthy volunteers. MRI scanning among study participants will resume as soon as pilot testing of the new magnet scanner is complete.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals.

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. **PRODUCTS:** List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Nothing to Report

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Nothing to Report

Other publications, conference papers, and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

> Nothing to Report

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

> Nothing to Report

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

> Nothing to Report

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

> Nothing to Report

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:
  - *data or databases;*
  - *biospecimen collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Example:

Name:	*Mary Smith*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*1234567*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support:	*The Ford Foundation (Complete only if the funding support is provided from other than this award).*

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Prime Site: NYU School of Medicine
PI: Charles Marmar, MD

Name: Charles Marmar, MD
Project Role: PI
Nearest person month worked: 2
Contribution to Project: Oversee and integrate all functions of the biological administrative core for the flow of subjects through all biological procedures, oversight of subject consent, preparation of progress reports, participation in weekly project meetings, and supervision of study personnel.

Name: Daniel Sodickson, MD, PhD
Project Role: Co-Investigator
Nearest person month worked: 2
Contribution to Project: Coordination of image processing core with UCSF to run imaging sequences on study participants, as well as oversaw the transfer of the imaging data to UCSF for processing.

Name: Duna Abu-Amara, MPH
Project Role: Sr. Project Manager
Nearest person month worked: 2
Contribution to Project: Project oversight, supervision of junior level Project Manager and Research Coordinators, coordination of information between investigators at each core site, monitored data and all regulatory requirements, submitted IRB materials, and participation in weekly project meetings.

Name: Emily Purchia, MPH
Project Role: Project Manager
Nearest person month worked: 2
Contribution to Project: Coordination and implementation of the regulatory paperwork, storage and shipment of urine and blood samples to Bronx VA, and attended weekly project meetings.

Name: Arsen Grigoryan, PhD
Project Role: Sr. Database Analyst
Nearest person month worked: 2
Contribution to Project: Daily maintenance of servers, log analysis, tuning, back-up, design, development, and support of data collection materials. Manage all of the tracking databases (subject tracking, specimen tracking, subject consent, subject contact, subject reimbursement, and IRB submission and approval database tracking), and attended weekly project meetings.

Name: Meng Qian, PhD
Project Role: Biostatistician
Nearest person month worked: 2
Contribution to Project: Oversaw the integration of the data from the project and cores, supervised data analyst, and junior level biostatistician, and attended weekly project meetings.

Name: Sisi Ma
Project Role: Scientific Programmer
Nearest person month worked: 2
Contribution to Project: Assist with all programming tasks and management of the data on the servers.

Name: Jennifer Newman, PhD
Project Role: Clinical Psychologist
Nearest person month worked: 2
Contribution to Project: Conducted structured diagnostic assessments and administered neurocognitive testing to participants;Responsible for scoring assessments and also attended weekly project and calibration meetings.

Laura Price
Project Role: Psychology Intern
Nearest person month worked: 1
Contribution to Project: Administered neurocognitive testing to participants; Responsible for scoring assessments and also attended weekly project and calibration meetings

Name: Anna Suessbrick, PhD
Project Role: Clinical Psychologist
Nearest person month worked: 2
Contribution to Project: Conducted structured diagnostic assessments and administered neurocognitive testing to participants; Responsible for scoring assessments and also attended weekly project and calibration meetings.

Site: NCIRE
Site PI: Michael Weiner, MD

Name: Michael Weiner, MD
Project Role: Site PI
Nearest person month worked: 2
Contribution to Project: Dr. Weiner oversees the development and conduct of work regarding the image processing core. Dr. Weiner provides overall supervision of the processing of data for the MRI research project and directs each stage of the investigation. He is also responsible for scientific guidance, interpretation of findings, and reporting results.

Name: Peter Ng
Project Role: Staff Research Associate I, Imaging Core
Nearest person months worked: 2
Contribution to Project: Mr. Ng assists in segmentation and volume measurements of MRI data, and performs data quality reviews on incoming data and process imaging data using the EMS segmentation method. He will also be processing imaging data using FreeSurfer software in order to obtain cortical thickness.

Site: UCSF
Site PI: Owen Wolkowitz, PhD

No work was performed at UCSF for this project as they are waiting for blood samples to be batched for analysis.
Thus, they have 0 efforts for all UCSF personnel at this quarter. The agreement was fully executed on June 16, 2014 and acknowledged in their system on June 18, 2014.

Site: Emory University
Site PI: Kerry Ressler, MD PhD

No work was performed at Emory for this project as they are waiting for blood samples to be batched for analysis. Thus, they have 0 efforts for all Emory personnel at this quarter.

Site: MSSM
Site PI: Rachel Yehuda, PhD

Name: Rachel Yehuda
Project Role: PI
Nearest person month worked: 2
Contribution to Project: Dr.Yehuda is the PI of the project.

Name: Janine Flory
Project Role: Co-Investigator
Nearest person month worked: 2
Contribution to Project: Dr. Flory provides day-to-day supervision of research staff and clinical interviewers, leading internal consensus meeting, and reviews data.

Name: Linda Bierer
Project Role: Co-Investigator
Nearest person month worked: 2
Contribution to Project: Dr. Bierer is the Medical Director and a Co-Investigator. She signs off on and reviews all clinical labs, along with reviewing the medical evaluations for all participants and reviewing data.

Name: Yusuf Henriques
Project Role: Research Health Scientist
Nearest person month worked: 2
Contribution to Project: Mr. Henriques is responsible for supplying personnel with study related materials, authorizing subject reimbursements, and oversight of grant and budget administration

Name: Amy Lehrner
Project Role: Clinical Psychologist
Nearest person month worked: 2
Contribution to Project: Dr. Lehrner has been responsible for completing 10 clinical interviews since 4/1/1 (including scoring and data review), and attends and contributes to all consensus meetings.

Name: Amy Ransohoff
Project Role: Clinical Research Coordinator
Nearest person month worked: 2

Name: Iouri Makotkine
Project Role: Lab Director
Nearest person month worked: 2
Contribution to Project: Oversees Freezerworks inventory, preparation for shipping, blood processing and assays, including supervision of lab personnel.

Name: Frank Desarnaud, PhD
Project Role: Lab Associate
Nearest person month worked: 2
Contribution to Project: Dr. Desarnaud has performed work in the area of DNA methylation, GENEWIZ and extraction from specimen collected from JJP VAMC and NYU.

Name: Aarti Bedi
Project Role: Lab Assistant
Nearest person month worked: 2
Contribution to Project: Responsible for inputting Freezerworks inventory, labeling, and preparation for shipping. Also responsible for blood and urine processing and running all associated assays.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to Report

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.
Provide the following information for each partnership:
<u>*Organization Name:*</u>
<u>*Location of Organization: (if foreign location list country)*</u>
<u>*Partner's contribution to the project*</u> *(identify one or more)*
- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS n/a

9. APPENDICES: attached

Validation Biomarkers for PTSD

At a Glance Recruitment Report

Grant Number: W81XWH-14-1-0043
PI: Charles Marmar
Report Period: 4/1/2014 – 4/14/2015

Table 1. Enrollment for Validating Biomarkers Recall and New Participants by Site

Values reported as: Number Enrolled/Target Number

Recruitment Site	Group	Q1	Q2	Q3	Q4	Year 1 Total
NYUMC	Recall PTSD +	2/2	1/2	0/2	0/2	3/8
	Recall PTSD -	4/3	3/3	3/3	4/3	14/12
	Recall Subthreshold	0	1	1	1	3
	New PTSD +	0/2	1/2	0/2	3/2	4/8
	New PTSD -	0/4	6/4	3/4	2/4	11/16
	Ineligible/Drop Outs	0	2	5	10	17
Total NYUMC		6/11	12 /11	7/11	10/11	35/44
JJPVAMC/MMSM	Recall PTSD +	2/3	1/3	3/3	0/3	6/12
	Recall PTSD -	0/2	2/2	2/2	3/2	7/8
	Recall Subthreshold	0	1	1	0	2
	New PTSD +	0/2	0/2	5/3	1/3	6/10
	New PTSD -	0/4	0/4	3/3	5/3	8/14
	Ineligible/Drop Outs	0	0	3	9	12
Total JJPVAMC/MMSM		2/11	4/11	14/11	9/11	29/44
Total by Quarter for NYUMC + JJPVAMC/MMSM		8/22	16/22	21/22	19/22	64/88

Table 2. Completed Procedures for Validating Biomarkers Recall Participants by Site

Recruitment Site	Procedure	Q1	Q2	Q3	Q4	Year 1 Total
NYUMC	BCI*	6	5	4	6	21
	Blood draw	0	8	4	4	16
	Self-report	0	7	4	4	15
	Brain imaging	1	8	5	0	14
	NCT**	0	7	4	4	15
JJPVAMC/MMSM	BCI*	2	4	6	3	15
	Blood draw	1	4	4	2	11
	Self-report	2	2	5	1	10
	Brain imaging	1	2	2	0	5
	NCT**	0	4	5	1	10

*BCI = Baseline Clinical Interview
**NCT = Neurocognitive Testing

Table 3. Completed Procedures for Validating Biomarkers New Participants by Site

Recruitment Site	Procedure	Q1	Q2	Q3	Q4	Year 1 Total
NYUMC	BCI*	0	9	8	14	31
	Blood draw	0	3	6	3	12
	Self-report	0	3	5	3	11
	Brain imaging	0	1	6	0	7
	NCT**	0	3	6	3	12
JJPVAMC/MMSM	BCI*	0	0	12	15	27
	Blood draw	0	0	5	5	10
	Self-report	0	0	4	7	11
	Brain imaging	0	0	1	0	1
	NCT**	0	1	3	6	10

*BCI = Baseline Clinical Interview
**NCT = Neurocognitive Testing

Validating Biomarkers for PTSD

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W81XWH-14-1-0043

PI: Charles R. Marmar, MD   **Org:** New York University   **Award Amount:** $2,480,000

Study/Product Aim(s)

• To validate candidate biomarkers for PTSD in OIF/OEF/OND Veterans from our discovery phase study. We will accomplish this aim by enrolling 35 new PTSD cases and 50 controls.
• To determine the relationship of longitudinal changes of biomarkers by reassessing 35 PTSD cases and 35 controls from our discovery phase (Time 0). The 35 cases and 35 controls will be reassessed 12 to 24 months after their initial assessment (Time 1).
• To ascertain biomarkers for PTSD from DoD maintained Archive Sera samples drawn before and after deployment for participants enrolled in the discovery and validation phases.
• To compare biomarkers for warzone related PTSD in male and female OEF and OIF veterans to determine common vs. gender specific markers and to contribute to the understanding of gender specific pathways for developing PTSD.

Approach

Biomarkers for PTSD study have been conducting a large multi-site consortium aimed at identifying biomarkers for PTSD. The consortium has succeeded in the implementation of a well-integrated system for collecting and analyzing clinical, behavioral, and biological data. We are beginning to elucidate potential candidate biomarkers for PTSD through a systems-biology approach. Our findings have revealed a number of candidate biomarkers. However, if these markers are to be translated into clinical practice it is essential that their reliability and stability are studied. This study will have three major aims: 1) To expand markers on a validation set of 35 male PTSD cases and 50 male controls. 2) To re-evaluate 35 cases and 35 controls from the discovery phase to test the stability over time. 3) To obtain 250 archived sera from PTSD/control participants, and identify pre-deployment omics markers.
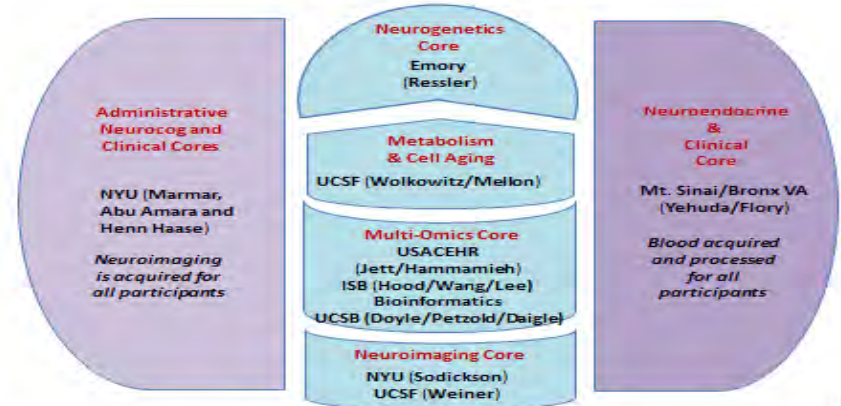
Accomplishment: IRB approvals have been obtained. To test the stability of the biomarkers, 35 participants from the discovery phase were re-evaluated. To test the validity of the markers 29 new participants were enrolled, of those 10 are PTSD+ and 19 PTSD- controls. Participants are being consented to access archived sera and a request to the Armed Forces Surveillance center of 158 samples was granted and samples were shipped to Dr. Jett's lab at Fort Detrick, MD.

Timeline and Cost

Activities	CY	14	15
Obtain IRB approvals to enroll participants. Obtain consent to access Archived Sera		�14	
Recruit Participants, collect data, request sera samples and ship to omic core		�14-15	
Analyze Data			▮
Disseminate results			▮
Estimated Budget ($M)		**$1.37M**	**$1.1M**
Updated: 4/14/15			

Goals/Milestones

CY14 Goal – **Acquire IRB Approvals. Obtain Consent to access archived Sera**
- ☑ Secure IRB approval from recruiting sites and HRPO
- ☑ Database Construction
- ☑ Hire and train personnel
- ☑ Obtain consent to access archived sera from enrolled participants
- ☑ Request first batch of pre-deployment and post deployment samples for 158 participants rom the Armed Forces Surveillance Center
- ☑ Ship samples to Dr. Jett's lab at Fort Detrick, MD

CY14-CY15 Goals – **Enrollment and Evaluation**
- ☐ Re-evaluate 35 cases and 35 controls from the discovery phase (in progress)
- ☐ Expand studying validity of markers on new 35 cases and 50 controls (in progress)
- ☐ Obtain archived sera samples, pre and post deployment on 250 participants (in progress)

CY15 Goal – **Data Analysis and Dissemination of Results**
- ☐ Conduct univariate and multivariate analyses to validate biomarkers for PTSD
- ☐ Conduct univariate and multivariate analyses to test the stability of biomarkers
- ☐ Conduct univariate and multivariate analyses on the archived sera samples
- ☐ Disseminate results in meetings, reports, publications briefings and conferences

Budget Expenditure to Date
Projected Expenditure: $2,480,000
Actual Expenditure: $689,061.34